Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1.-30. (Cancelled)

31. (Previously Presented) A cultured skin construct having at least two layers, comprising:

(a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix which is synthesized and assembled by the cultured fibroblast cells, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) type I and type III collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) decorin;

(iii) fibronectin,

(iv) tenascin; and,

(v) glycosaminoglycans;

wherein said extracellular matrix is produced by the cultured dermal fibroblast cells in the absence of exogenous matrix components during the culturing conditions; and,

(b) a second layer of keratinocyte cells disposed on the first layer to form an epidermal cell layer, wherein the epidermal cell layer is multilayered, stratified, differentiated and exhibits a basal layer, suprabasal layer, a granular layer and a stratum corneum;

and wherein the bilayered cultured skin construct has a basement membrane present at the junction of the first and second layers.

32. (Previously Presented) The cultured skin construct of claim 31, wherein said cultured cells are cultured in chemically defined media.

33. (Previously Presented) The cultured skin construct of claim 31, wherein said first layer has cultured cells from dermal papilla of hair follicles localized on said first layer.

34. (Previously Presented) The cultured skin construct of claim 31, wherein the cultured dermal fibroblast cells are genetically modified to produce extracellular matrix components.

35. (Previously Presented) The cultured skin construct of claim 31, wherein the cultured dermal fibroblast cells are genetically modified to produce a growth factor, hormone, peptide, or protein.

36. (Currently Amended) The cultured skin construct of any of claims 31-35, wherein the construct is cohesive in having physical unitary integrity ~~and tissue-like handling properties~~.

37. (Previously Presented) A cultured skin construct having at least two layers, comprising:

(a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix which is synthesized and assembled by the cultured fibroblast cells, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) type I and type III collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) decorin;

(iii) fibronectin,

(iv) tenascin; and,

(v) glycosaminoglycans;

wherein said extracellular matrix is produced by the cultured dermal fibroblast cells in the absence of exogenous matrix components during the culturing conditions; and,

(b) a second layer of cells comprising epithelial cells disposed on the first layer.

38. (Previously Presented) The cultured skin construct of claim 37, wherein the epithelial cells are selected from the group consisting of keratinocytes, corneal epithelial cells, epithelial cells from oral mucosa, esophageal epithelial cells, and uroepithelial cells.

39. (Previously Presented) A cultured tissue construct having at least three layers, comprising:

(a) a first layer of cultured fibroblasts cells which produce a layer of extracellular matrix which is synthesized and assembled by the cultured fibroblast cells, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) fibrillar collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) decorin; and,

(iii) glycosaminoglycans;

wherein said extracellular matrix is produced by the cultured fibroblast cells in the absence of exogenous matrix components during the culturing conditions;

(b) a second layer of cells comprising epithelial cells disposed on the first layer; and,

(c) a third layer of cells disposed on the second layer of epithelial cells.

40. (Previously Presented) The cultured tissue construct of claim 39, wherein said fibroblast cells contained within said first layer are derived from tissue selected from the group consisting of neonate male foreskin, dermis, tendon, lung, cartilage, urethra, corneal stroma, oral mucosa, umbilical cord, and intestine.

41. (Previously Presented) The cultured tissue construct of claim 39, wherein said fibroblast cells contained within said first layer are dermal fibroblasts.

42. (Previously Presented) The cultured tissue construct of claim 39, wherein said first layer has cultured cells from dermal papilla of hair follicles localized on said first layer.

43. (Previously Presented) The cultured tissue construct of claim 39, wherein said cultured cells are cultured in chemically defined media.

44. (Previously Presented) The cultured tissue construct of claim 39, wherein the cultured fibroblast cells are genetically modified to produce extracellular matrix components.

45. (Previously Presented) The cultured tissue construct of claim 39, wherein the cultured fibroblast cells are genetically modified to produce a growth factor, hormone, peptide, or protein.

46. (Previously Presented) The cultured tissue construct of claim 39, wherein the epithelial cells are selected from the group consisting of keratinocytes, corneal epithelial cells, epithelial cells from oral mucosa, esophageal epithelial cells, and uroepithelial cells.

47. (Currently Amended) The cultured tissue construct of any of claims 39-46, wherein the construct is cohesive in having physical unitary integrity ~~and tissue-like handling properties~~.

48. (Currently Amended) A method for producing a cultured tissue construct, comprising,

(a) seeding fibroblast cells capable of synthesizing an extracellular matrix on a porous membrane in a culture vessel in a cell culture medium at about 80% to about 100% confluence;

(b) stimulating the fibroblast cells to synthesize, secrete and organize extracellular matrix components ~~in a second culture medium~~; and,

(c) continued culturing of the fibroblast cells until the cells form a layer of synthesized extracellular matrix of at least about 30 microns thick, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) fibrillar collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) tenascin; and,

(iii) glycosaminoglycans;

and wherein said extracellular matrix is produced by the cultured fibroblast cells in the absence of exogenous matrix components during the culturing conditions.

49. (Previously Presented) The method of claim 48, wherein the fibroblast cells are derived from tissue selected from the group consisting of neonate male foreskin, dermis, tendon, lung, cartilage, urethra, corneal stroma, oral mucosa, umbilical cord, and intestine.

50. (Previously Presented) A method for transplantation or implantation of a cultured skin construct into a patient comprising transplanting or implanting into a patient, a cultured skin construct having at least two layers, comprising:

(a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix which is synthesized and assembled by the cultured fibroblast cells, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) type I and type III collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) decorin;

(iii) fibronectin,

(iv) tenascin; and,

(v) glycosaminoglycans;

wherein said extracellular matrix is produced by the cultured dermal fibroblast cells in the absence of exogenous matrix components during the culturing conditions; and,

(b) a second layer of keratinocyte cells disposed on the first layer to form an epidermal cell layer, wherein the epidermal cell layer is multilayered, stratified, differentiated and exhibits a basal layer, suprabasal layer, a granular layer and a stratum corneum;

and wherein the bilayered cultured skin construct has a basement membrane present at the junction of the first and second layers.

51. (Previously Presented) A method for transplantation or implantation of a cultured skin construct into a patient comprising transplanting or implanting into a patient, a cultured skin construct having at least two layers, comprising:

(a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix which is synthesized and assembled by the cultured fibroblast cells, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) type I and type III collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) decorin;

(iii) fibronectin,

(iv) tenascin; and,

(v) glycosaminoglycans;

wherein said extracellular matrix is produced by the cultured dermal fibroblast cells in the absence of exogenous matrix components during the culturing conditions; and,

(b) a second layer of cells comprising epithelial cells disposed on the first layer.

52. (Previously Presented) A method for transplantation or implantation of a cultured tissue construct into a patient comprising transplanting or implanting into a patient, a cultured tissue construct having at least three layers, comprising:

(a) a first layer of cultured fibroblasts cells which produce a layer of extracellular matrix which is synthesized and assembled by the cultured fibroblast cells, with the cultured fibroblast cells contained within the synthesized extracellular matrix layer, wherein the extracellular matrix comprises:

(i) fibrillar collagen showing a packing organization of fibrils and fibril bundles exhibiting a quarter-staggered 67 nm banding pattern;

(ii) decorin; and,

(iii) glycosaminoglycans;

wherein said extracellular matrix is produced by the cultured fibroblast cells in the absence of exogenous matrix components during the culturing conditions;

(b) a second layer of cells comprising epithelial cells disposed on the first layer; and,

(c) a third layer of cells disposed on the second layer of epithelial cells.

53. (New) The cultured skin construct of claims 31 or 37, wherein the fibroblast cells are cultured in a matrix production medium to produce the layer of extracellular matrix.

54. (New) The cultured skin construct of claim 53, wherein the matrix production medium comprises an ascorbate derivative.

55. (New) The cultured skin construct of claim 54, wherein the ascorbate derivative is selected from the group consisting of sodium ascorbate, ascorbic acid or a derivative thereof.

56. (New) The cultured skin construct of claim 54, wherein the matrix production medium further comprises epidermal growth factor, hydrocortisone, ethanolamine, o-phosphoryl-ethanolamine, insulin, transferring, triiodothyronine, selenium, L-ascorbic acid, L-proline, glycine or combinations thereof.

57. (New) The cultured tissue construct of claim 39, wherein the fibroblast cells are cultured in a matrix production medium to produce the layer of extracellular matrix.

58. (New) The cultured tissue construct of claim 57, wherein the matrix production medium comprises an ascorbate derivative.

59. (New) The cultured tissue construct of claim 58, wherein the ascorbate derivative is selected from the group consisting of sodium ascorbate, ascorbic acid or a derivative thereof.

60. (New) The cultured tissue construct of claim 58, wherein the matrix production medium further comprises epidermal growth factor, hydrocortisone, ethanolamine, o-phosphoryl-ethanolamine, insulin, transferring, triiodothyronine, selenium, L-ascorbic acid, L-proline, glycine or combinations thereof.

61. (New) The method of claim 48, wherein stimulating the fibroblast cells comprises culturing them in a matrix production medium to produce the layer of extracellular matrix.

62. (New) The method of claim 61, wherein the matrix production medium comprises an ascorbate derivative.

63. (New) The method of claim 62, wherein the ascorbate derivative is selected from the group consisting of sodium ascorbate, ascorbic acid or a derivative thereof.

64. (New) The method of claim 62, wherein the matrix production medium further comprises epidermal growth factor, hydrocortisone, ethanolamine, o-phosphoryl-ethanolamine, insulin, transferring, triiodothyronine, selenium, L-ascorbic acid, L-proline, glycine or combinations thereof.

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A prosthesis comprising two or more superimposed, chemically bonded layers of processed tissue material which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells; ~~and~~

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse; and

wherein the prosthesis is selected from a hernia repair patch, a femoral hernia repair plug, a pericardial patch, a bladder sling, a uterus sling, an intra-cardiac patch, a replacement heart valve, a vascular patch, an annular fibrosis repair plug, an annular fibrosis repair patch, a rotator cuff repair prosthesis, a dura mater repair patch, a cystocele repair device, a retrocele repair device, a vaginal vault prolapse repair sling, and a plastic surgery implant.

2. (Cancelled)

3. (Currently Amended) The prosthesis of claim [[2]]1 wherein said prosthesis is chemically bonded with the crosslinking agent 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride.

4. (Cancelled)

5. (Cancelled)

6. (Cancelled)

7. (Currently Amended) A method of repairing or replacing a damaged tissue comprising implanting a prosthesis in a patient comprising two or more superimposed, bonded layers of processed tissue material which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells; ~~and~~

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse; and

wherein the prosthesis is selected from a hernia repair patch, a femoral hernia repair plug, a pericardial patch, a bladder sling, a uterus sling, an intra-cardiac patch, a replacement heart valve, a vascular patch, an annular fibrosis repair plug, an annular fibrosis repair patch, a rotator cuff repair prosthesis, a dura mater repair patch, a cystocele repair device, a retrocele repair device, a vaginal vault prolapse repair sling, and a plastic surgery implant.

8. (Cancelled)

9. (Cancelled)

10. (Currently Amended) A method for treating a damaged or diseased ~~soft~~ tissue ~~in need of repair~~, comprising implantation of a prosthesis comprising two or more superimposed, chemically bonded layers of processed tissue material derived from the tunica submucosa of small intestine which, when implanted on the damaged or diseased ~~soft~~ tissue, undergoes controlled biodegradation occurring with adequate

living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells; ~~and~~

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse; and

wherein the prosthesis is selected from a hernia repair patch, a femoral hernia repair plug, a pericardial patch, a bladder sling, a uterus sling, an intra-cardiac patch, a replacement heart valve, a vascular patch, an annular fibrosis repair plug, an annular fibrosis repair patch, a rotator cuff repair prosthesis, a dura mater repair patch, a cystocele repair device, a retrocele repair device, a vaginal vault prolapse repair sling, and a plastic surgery implant.

11. (Currently Amended) The method of claim 10, wherein the prosthesis ~~damaged or diseased soft tissue in need of repair~~ is used for a treatment selected from ~~the group consisting of~~ treating defects of the abdominal and thoracic wall, muscle flap reinforcement, rectal and vaginal prolapse, reconstruction of the pelvic floor, ~~hernias~~ hernia repair, suture-line reinforcement and reconstructive procedures.

12. (Original) The method of claim 10, wherein the prosthesis comprises five sheets of processed intestinal collagen derived from the tunica submucosa of small intestine which are bonded and crosslinked together with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride at a concentration between 0.1 to 100 mM.

13. (Cancelled)

14. (Cancelled)

15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (Cancelled)

19. (Cancelled)

20. (Currently Amended) A prosthesis comprising two or more superimposed, chemically bonded layers of processed tissue material which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells, ~~and~~ wherein the processed tissue material contains less than about 5% glycoproteins, glycosaminoglycans, proteoglycans, lipids, non-collagenous proteins, and nucleic acids by dry weight, and wherein the prosthesis is selected from a hernia repair patch, a femoral hernia repair plug, a pericardial patch, a bladder sling, a uterus sling, an intra-cardiac patch, a replacement heart valve, a vascular patch, an annular fibrosis repair plug, an annular fibrosis repair patch, a rotator cuff repair prosthesis, a dura mater repair patch, a cystocele repair device, a retrocele repair device, a vaginal vault prolapse repair sling, and a plastic surgery implant.

21. (New) An intra-cardiac patch comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted intra-cardiac patch is remodeled by the patient's living cells; and

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse.

22. (New) A replacement heart valve comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted replacement heat valve is remodeled by the patient's living cells; and

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse.

23. (New) A rotator cuff repair prosthesis comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted rotator cuff repair prosthesis is remodeled by the patient's living cells; and

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse.

24. (New) A dura mater repair patch comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled

biodegradation occurring with adequate living cell replacement such that the original implanted dura mater repair patch is remodeled by the patient's living cells; and

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse.

25. (New) A prosthesis comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells;

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse; and

wherein the prosthesis is selected from a bladder sling, a uterus sling, and a vaginal vault prolapse repair sling.

26. (New) A plastic surgery implant comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted plastic surgery implant is remodeled by the patient's living cells; and

wherein the processed tissue material is chemically cleaned using:

(a) an effective amount of chelating agent under alkaline conditions,

(b) an effective amount of acid containing a salt,

(c) an effective amount of buffered salt solution, and

(d) a rinse.

WHAT IS CLAIMED:

1. A prosthesis comprising two or more superimposed, bonded layers of collagenous tissue which have been crosslinked with a crosslinking agent that permits bioremodeling and sterilized, wherein all of the layers of the prosthesis are completely bioremodelable, and which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

2. The prosthesis of claim 1 wherein the shape of said prosthesis is flat, tubular, or complex.

3. The prosthesis of claim 1 wherein said collagen material is sourced from a mammalian source and is intestinal material, fascia lata, dura mater, and pericardium.

4. The prosthesis of claim 3 wherein said collagen material is the tunica submucosa of the small intestine.

5. The prosthesis of claim 1 wherein said collagen layers are bonded together by heat welding for a time and under conditions sufficient to effect the bonding of the collagenous tissue layers.

6. The prosthesis of claim 1 wherein said prosthesis is crosslinked with the crosslinking agent 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride.

7. The prosthesis of claim 6 wherein sulfo-N-hydroxysuccinimide is added to the crosslinking agent.

8. The prosthesis of claim 6 wherein acetone is added to the crosslinking agent.

9. The prosthesis of claim 1 wherein the prosthesis is sterilized with peracetic acid.

10. The prosthesis of claim 10 wherein said prosthesis is non-antigenic.

11. The prosthesis of claim 1 wherein one or more surfaces of said prosthesis is coated with a collagenous material which acts as a smooth flow surface.

12. The prosthesis of claim 1 wherein said prosthesis further contains pores.

13. The prosthesis of claim 1 wherein said prosthesis is further composed of chopped collagen fibers.

14. The prosthesis of claim 1 wherein said prosthesis is further composed of collagen threads.

15. The prosthesis of claim 14 wherein said collagen threads are arranged to form a felt, a bundle, a weave or a braid.

16. The prosthesis of any of claims 13-15 wherein said collagen fibers or threads are partially or completely crosslinked.

17. The prosthesis of claim 1 wherein said prosthesis additionally contains an anticoagulant; one or more antibiotics, or one or more growth factors.

18. A method of preparing a prosthesis having two or more superimposed, bonded layers of collagen material, comprising:

(a) bonding the two or more collagen layers together using heat welding by heating said collagenous tissue layers for a time and under conditions sufficient to effect the bonding of the collagen layers and to form a prosthesis;

(b) cooling said heated prosthesis; and,

(c) crosslinking said prosthesis with a crosslinking agent that permits bioremodeling, wherein said thus formed prosthesis when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells;

wherein the collagenous tissue layers are sterilized with peracetic acid before bonding in step (a) or the prosthesis is sterilized after crosslinking in step (c).

19. The method of claim 18 wherein said collagen layers are formed from two or more layers of collagenous tissue sourced from a mammalian source and is intestinal material, fascia lata, dura mater, and pericardium.

20. The method of claim 19 wherein said collagen material is the tunica submucosa of the small intestine.

21. The method of claim 18 wherein said heat welding is from about 50°C to about 75°C, more preferably from about 60° to 65°C and most preferably at about 62°C.

22. The method of claim 18 wherein said cooling is accomplished by quenching.

23. The method of claim 18 wherein said heat welding is accomplished for a time from about 7 minutes to about 24 hours, preferably about 1 hour.

24. The method of claim 18 wherein said prosthesis is crosslinked with the crosslinking agent 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride.

25. The method of claim 18 wherein said prosthesis is non-antigenic.

26. A method of repairing or replacing a damaged tissue comprising implanting a prosthesis in a patient comprising two or more superimposed, bonded layers of collagenous tissue which have been sterilized with peracetic acid and crosslinked with a crosslinking agent that permits bioremodeling, wherein all of the layers of the prosthesis are completely bioremodelable, and which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

27. A sterile, non-pyrogenic, and non-antigenic prosthesis formed from mammalian derived collagenous tissue for engraftment to a recipient patient, whereby said engrafted prosthesis does not elicit a humoral immune response to components in said collagenous tissue and wherein said prosthesis concomitantly undergoes bioremodeling occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

28. The prosthesis if claim 27 wherein said humoral immune response to components derived from said collagenous tissue demonstrates no significant increase in antibody titer for antibodies from baseline titer levels when blood serum obtained from a

recipient of a prosthesis is tested for antibodies to proteins in extracts of the collagenous tissue..

29. The prosthesis of claim 28 wherein said antibody titer levels is 1:40 or less for a patient or host previously non-sensitized to collagenous tissue proteins.

30. A method of preparing a non-antigenic prosthesis prepared from collagenous tissue derived from a mammalian source selected from the group consisting of intestinal material, fascia lata, dura mater, and pericardium, comprising:

(a) disinfecting the collagen material with peracetic acid at a concentration between about 0.01 and 0.3% v/v in water; and,

(b) crosslinking said sterilized collagenous tissue with a crosslinking agent that permits bioremodeling;

wherein the prosthesis isformed from two or more superimposed, bonded layers of collagenous tissue, wherein all of the layers of the prosthesis are bioremodelable, and wherein the prosthesis when implanted into a mammalian patient, undergoes controlled bioremodeling occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells without eliciting a significant humoral immune response.

31. The method of claim 30 wherein said collagenous tissue is the tunica submucosa of the small intestine.

32. The method of claim 30 wherein said collagen material is formed from two or more layers of superimposed, bonded layers of collagen material.

33. The method of claim 30 wherein the prosthesis is sterilized with peracetic acid prior to implantation into the mammalian patient.

WE CLAIM:

1. A bioremodelable tubular prosthesis comprising a first layer of processed tissue matrix formed into a tube having a luminal surface and abluminal surface and a second layer of dense fibrillar collagen on the luminal surface of the first layer.

2. A bioremodelable tubular prosthesis comprising a first layer of processed tissue matrix formed into a tube having a luminal surface and abluminal surface wherein opposing edges of the layer overlap to form a bonding region between about 5% and 20% of the circumference of the tube and a second layer of dense fibrillar collagen on the luminal surface of the first layer.

3. The bioremodelable tubular prosthesis of claims 1 and 2 wherein the processed tissue matrix is derived from the tunica submucosa of small intestine.

4. The bioremodelable tubular prosthesis of claims 1 and 2 wherein the prosthesis is crosslinked with EDC.

5. A method for producing a bioremodelable prosthetic tube construct comprising at least two layers of processed tissue matrix wherein the method comprises:

(a) flagging the processed tissue matrix around a sleeve-covered mandrel by hydrating one edge of the processed tissue matrix and contacting the sleeve-covered mandrel to the hydrated edge of the processed tissue matrix;

(b) drying the processed tissue matrix to the sleeve-covered mandrel;

(c) rehydrating the processed tissue matrix with a hydrating agent to form hydrated processed tissue matrix;

(d) rotating the mandrel twice to wrap the hydrated processed tissue matrix to form two wrapped hydrated layers of processed tissue matrix;

(e) dehydrating the layers of the processed tissue matrix;

(f) removing the processed tissue matrix from the mandrel;

(g) contacting the processed tissue matrix with a crosslinking agent to crosslink the collagen.

(h) depositing a dense fibrillar collagen layer on the luminal surface of the tube.

6. A method for replacing a damaged or diseased portion of vasculature with a bioremodelable tubular prosthesis comprising a two layers of processed tissue matrix and a layer

of dense fibrillar collagen on the luminal surface of the tubular prosthesis wherein the method comprises:

(a) anastomosizing a segment of vasculature;

(b) removing the segment of vasculature;

(c) replacing the segment of removed vasculature with a bioremodelable tubular prosthesis;

(d) suturing the bioremodelable tubular prosthesis; and,

(e) removing the anastomoses to resume blood flow.

WE CLAIM:

1. A prosthesis comprising two or more superimposed, chemically bonded layers of processed tissue material which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

2. A prosthesis comprising two or more superimposed, chemically bonded layers of processed tunica submucosa of small intestine which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

3. The prosthesis of claim 2 wherein said prosthesis is chemically bonded with the crosslinking agent 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride.

4. The method of preparing a prosthesis having two or more superimposed, bonded layers of processed tissue matrix, comprising:

(a) layering two or more sheets of hydrated processed tissue layers;

(b) dehydrating said tissue layers to adhere the layers together;

(c) crosslinking said tissue layers with a crosslinking agent to bond the layers together; and,

(d) rinsing said layers to remove the crosslinking agent;

wherein said thus formed prosthesis when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

5. The method of claim 4 wherein said processed tissue matrix is derived from the tunica submucosa of the small intestine.

6. The method of claim 5 wherein the tunica submucosa is essentially acellular telopeptide collagen.

7. A method of repairing or replacing a damaged tissue comprising implanting a prosthesis in a patient comprising two or more superimposed, bonded layers of collagen material which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

8. The method of claim 7 wherein the prosthesis is a hernia repair patch, a pericardial patch, a bladder sling, a uterus sling, intra-cardiac patch, replacement heart valve or a vascular patch.

We claim:

1. A bioremodelable prosthesis comprising a collagen tube comprising at least one layer of processed tissue matrix of crosslinked submucosal collagen of small intestine.

2. The bioremodelable prosthesis of claim 1, wherein the prosthesis functions as a remodeling template for the ingrowth of host cells.

3. The bioremodelable prosthesis of claim 1, wherein the processed tissue matrix is bonded to itself or another layer of processed tissue matrix.

4. The bioremodelable prosthesis of claim 1, wherein the processed tissue matrix is derived from the tunica submucosa of mammalian small intestine.

5. The bioremodelable prosthesis of claim 4, wherein the processed tissue matrix is derived from the tunica submucosa of porcine small intestine.

6. The bioremodelable prosthesis of claim 1, wherein the collagen tube comprises at least two layers of processed tissue matrix of crosslinked submucosal collagen.

7. The bioremodelable prosthesis of claim 6, wherein the layers are derived from the same material.

8. The bioremodelable prosthesis of claim 6, wherein the layers are derived from the different collagen materials.

9. The bioremodelable prosthesis of claim 6, wherein the layers are crosslinked.

10. The bioremodelable prosthesis of claim 1, wherein the collagen tube defines a lumen having a luminal surface, wherein the processed tissue matrix has a mucosal surface and a serosal surface, and wherein the mucosal surface of the innermost layer of processed tissue matrix is the luminal surface of the collagen tube.

11. The bioremodelable prosthesis of claim 1, wherein the bioremodelable prosthesis is an external vein support.

12. The bioremodelable prosthesis of claim 1, wherein the bioremodelable prosthesis is a neuron growth tube.

13. A bioremodelable prosthesis comprising a collagen tube comprising at least one layer of processed tissue matrix of crosslinked submucosal collagen of small intestine, wherein the prosthesis functions as a remodeling template for the ingrowth of host cells, wherein the prosthesis is pliable, suturable, non-creeping, semi-permeable, and non-porous, and wherein the prosthesis is sterilized.

14. A bioremodelable external vein support comprising a collagen tube comprising at least one layer of processed tissue matrix of crosslinked submucosal collagen of small intestine.

15. The bioremodelable external vein support of claim 14, wherein collagen tube defines a lumen having a luminal surface, wherein the processed tissue matrix has a mucosal surface and a serosal surface, and wherein the mucosal surface of the innermost layer of processed tissue matrix is the luminal surface of the collagen tube.

16. A neuron growth tube comprising a collagen tube comprising at least one layer of processed tissue matrix of crosslinked submucosal collagen of small intestine.

17. The neuron growth tube of claim 16, wherein the neuron growth tube functions to guide nerve regeneration.

18. The neuron growth tube of claim 16, wherein the neuron growth tube contains extracellular matrix components, at least one growth factor, cultured cells, or a combination thereof.

WE CLAIM:

1. A bioremodelable tubular prosthesis comprising a single layer of processed tissue matrix formed into a tube which, when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

2. A bioremodelable tubular prosthesis comprising a first layer of processed tissue matrix formed into a tube wherein opposing edges of the layer overlap to form a bonding region between about 5% to 20% of the circumference of the tube which, when implanted into a mammalian patient patient, undergoes controlled biodegradatoin occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

3. The bioremodelable tubular prosthesis of claims 1 and 2 wherein the processed tissue matrix is derived from the tunica submucosa of small intestine.

4. The bioremodelable tubular prosthesis of claims 1 and 2 wherein the bonding region is crosslinked with EDC.

5. A method for producing a bioremodelable prosthetic tube construct comprising two layers of processed tissue matrix wherein the method comprises:

(a) flagging the processed tissue matrix around a sleeve-covered mandrel by hydrating one edge of the processed tissue matrix and contacting the sleeve-covered mandrel to the hydrated edge of the processed tissue matrix;

(b) drying the processed tissue matrix to the sleeve-covered mandrel;

(c) rehydrating the processed tissue matrix with a hydrating agent to form hydrated processed tissue matrix;

(d) rotating the mandrel twice to wrap the hydrated processed tissue matrix to form two wrapped hydrated layers of processed tissue matrix;

(e) dehydrating the layers of the processed tissue matrix; and

(f) contacting the layers of the processed tissue matrix with a crosslinking agent to crosslink the collagen.

6. A method for repairing or replacing a damaged tissue comprising implanting a prosthesis in a ptient comprising a layer of processed tissue matrix formed into a tube which, when when implanted into a mammalian patient, undergoes controlled biodegradation occurring with adequate living cell replacement such that the original implanted prosthesis is remodeled by the patient's living cells.

1. A bioremodelable collagenous tissue matrix composition derived from native tissue, comprising:

telopeptide collagen;

elastin, wherein elastin is less than 10% of the total composition based on dry weight; and

non-collagenous and non-elastinous components, wherein said components are less than 5% of the total composition based on dry weight;

wherein the collagenous tissue matrix is free of detergent residues, enzymatic modification, endotoxin and cells and cellular debris; and

wherein the native tissue is selected from the group consisting of dermis, artery, vein, pericardium, heart valve, dura mater, ligament, bone, cartilage, fascia and intestine.

2. The bioremodelable collagenous tissue matrix composition of claim 1, wherein the collagenous tissue matrix is sterile.

3. A bioremodelable collagenous tissue matrix composition derived from small intestine, comprising:

telopeptide collagen;

elastin, wherein elastin is less than 10% of the total composition based on dry weight; and

non-collagenous and non-elastinous components, wherein said components are less than 5% of the total composition based on dry weight; and

wherein the collagenous tissue matrix is free of detergent residues, enzymatic modification, endotoxin and cells and cellular debris.

4. The bioremodelable collagenous tissue matrix composition of claim 3, wherein the collagenous tissue matrix is derived from the tunica submucosa of small intestine.

5. The bioremodelable collagenous tissue matrix composition of claim 3, wherein the collagenous tissue matrix is chemically cleaned.

6. The bioremodelable collagenous tissue matrix composition of claim 3, wherein the collagenous tissue matrix is sterile.

7. The bioremodelable collagenous tissue matrix composition of claim 3, wherein the collagenous tissue matrix is layered and bonded together to form multilayer sheets, tubes, or complex shaped prostheses.

8. The bioremodelable collagenous tissue matrix composition of claim 7, wherein the collagenous tissue matrix is crosslinked.

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List of Pending Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-5. (Cancelled)

6. (Previously Presented) A bioremodelable prosthesis for treating a patient with a diseased or damaged organ, comprising a first layer that contains acid-extracted fibrillar or non-fibrillar collagen, and a second layer derived from the tunica submucosa of the small intestine that provides structural stability, is pliable, and is semi-permeable, wherein said prosthesis all undergoes controlled biodegradation occurring with adequate living cell replacement such that the original prosthesis is replaced by the patient's living cells.

7. (Previously Presented) The prosthesis of claim 6, wherein the prosthesis is tubular and the diseased or damaged organ is an artery or a vein.

8. (Previously Presented) The prosthesis of claim 7, wherein the tubular prosthesis has a diameter of less than 6 mm.

9. (Previously Presented) The prosthesis of claim 7, wherein the tubular prosthesis has a diameter of between 6 to 12 mm.

10. (Previously Presented) The prosthesis of claim 7, wherein the tubular prosthesis has a diameter of greater than 12 mm.

11. (Previously Presented) The prosthesis of claim 6, wherein the diseased or damaged organ is the esophagus, intestine, bowel, urethra, or fallopian tubes.

12. (Previously Presented) The prosthesis of claim 6, wherein said first layer has a smooth flow surface.

13. (Previously Presented) The prosthesis of claim 12, wherein the smooth flow surface is thrombosis-resistant.

14. (Previously Presented) The prosthesis of claim 6, wherein said second layer is crosslinked.

15. (Previously Presented) The prosthesis of claim 14, wherein said second layer is crosslinked with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC).

16. (Previously Presented) The prosthesis of claim 6, wherein said second layer has a thickness of between about 50 microns to about 150 microns.

17. (Previously Presented) The prosthesis of claim 6, wherein the tunica submucosa of the small intestine is mechanically cleaned to remove the tunica muscularis and the tunica mucosa.

18. (Previously Presented) The prosthesis of claim 17, wherein said mechanically cleaned tunica submucosa is chemically cleaned.

19. (Previously Presented) The prosthesis of claim 6, wherein the tunica submucosa of the small intestine is sterilized.

20. (Previously Presented) The prosthesis of claim 6, wherein said prosthesis further comprises a third layer.

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21. (Previously Presented) The prosthesis of claim 6, wherein the first layer is on the inside of the prosthesis.

22. (Previously Presented) The prosthesis of claim 6, wherein the second layer is on the inside of the prosthesis.

23. (Previously Presented) The prosthesis of claim 6, wherein the prosthesis is treated with a drug.

24. (Previously Presented) The prosthesis of claim 6, wherein the first layer is treated with a drug.

25. (Previously Presented) The prosthesis of claim 6, wherein the second layer is treated with a drug.

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26. (Previously Presented) The prosthesis of claim 23, 24, or 25, wherein the drug is heparin.

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27. (Previously Presented) The prosthesis of claim 23, 24, or 25, wherein the drug is a growth factor.